Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (currently amended) A method for identifying a macromolecule having a sequence and sequence modifications thereof from mass spectrometry data comprising:

(a) providing at least one *de novo* sequence from mass spectrometry data of sequences of fragments of said macromolecule to a computer-based system that implements the identification of sequences of molecules and sequence modifications from mass spectrometry data,

(b) calculating at least one mass-based alignment between said at least one *de novo* sequence and sequences in a sequence database, wherein the molecular masses of said fragments in a *de novo* sequence are compared to molecular masses of fragments in each sequence in said sequence database,

(c) interpreting mass differences between a sequence in the sequence database and the at least one *de novo* sequence using a modification catalog, said mass differences having been identified within said mass-based alignment,

wherein said modification catalog contains information for accurately identifying sequence variations and post-translational protein modifications,

(d) calculating at least one match score for the mass-based alignment that provides an indication of matching between a sequence in the sequence database and the at least one *de novo* sequence,

(e) identifying sequences in the sequence database from mass-based alignments in response to the match scores,

(f) grouping identifications of sequences in the sequence database from at least one *de novo* sequence into an identified macromolecule list that agrees with the *de novo* sequencing results, and

(g) storing said macromolecule list on a computer readable medium.

2. (previously presented) The method of claim 1, wherein the mass spectrometry data are generated from a tandem mass spectrometer device.

3. (previously presented) The method of claim 1, wherein at least one *de novo* sequence is an estimated sequence of fragments generated from the mass spectrometry data.

4. (previously presented) The method of claim 3, wherein a *de novo* sequence is a complete or partial sequence of fragments.

5. (previously presented) The method of claim 3, wherein a *de novo* sequence contains ambiguous mass regions of molecules where the exact sequence of fragments cannot be determined.

6. (previously presented) The method of claim 5, wherein a mass region is the molecular mass of the fragments in an unidentifiable region of molecules.

7. (previously presented) The method of claim 1, wherein at least one fragment is an amino acid and at least one sequence of fragments is a peptide.

8. (original) The method of claim 7, wherein the peptides are derived by an enzymatic digestion of proteins.

9. (original) The method of claim 7, wherein the sequence database is a database of amino acid sequences of proteins.

10. (original) The method of claim 7, wherein the sequence database is a database of amino acid sequences derived from nucleotide sequences.

11. (original) The method of claim 7, wherein the sequence database is a database of *de novo* peptide sequences.

12. (previously presented) The method of claim 7, wherein the sequence in the sequence database is a particular amino acid sequence.

13. (previously presented) The method of claim 6, further comprising:

(h) identifying a sequence in the sequence database with a tag match, and

(i) generating a mass-based alignment between a *de novo* sequence and the sequence in the sequence database.

14. (original) The method of claim 13, wherein a mass-based alignment is a series of consecutive local mass-based alignments on either side of a tag match.

15. (original) The method of claim 14, wherein a tag match is when a tag in the *de novo* sequence has been shown to be equivalent to a tag in a sequence in the sequence database by way of a tag search.

16. (original) The method of claim 15, wherein a tag search is used to identify a subset of sequences in the sequence database from which to compute mass-based alignments.

17. (previously presented) The method of claim 16, wherein a tag is a sequence of consecutive fragments of a specified length, wherein the specified length is 2 to 4 fragments.

18. (previously presented) The method of claim 16, wherein single fragments of the tag and sequences in the sequence database that have the same nominal weight are represented by a single fragment.

19. (previously presented) The method of claim 14, wherein fragments at either side of the tag match in both the *de novo* sequence and the sequence of the sequence database are converted into mass objects.

20. (original) The method of claim 19, wherein a mass object is at least one molecular mass and a name for that mass.

21. (previously presented) The method of claim 18, wherein for single fragments, mass objects are assigned the molecular mass of the single fragment.

22. (original) The method of claim 18, wherein for unidentifiable mass regions, mass objects are assigned the molecular mass of the unidentifiable mass region.

23. (original) The method of claim 18, wherein for reference amino acids, which represent multiple amino acids, mass objects are assigned the molecular mass of each amino acid.

24. (original) The method of claim 19, wherein for variably modified amino acids, mass objects are assigned multiple molecular masses.

25. (previously presented) The method of claim 19, wherein mass regions are treated as single fragments with a single molecular mass.

26. (previously presented) The method of claim 19, wherein a gap is a mass object of zero molecular mass that represents no fragment.

27. (original) The method of claim 19, wherein a local mass-based alignment is a matching of at least one consecutive mass object in the sequence in the sequence database and at least one consecutive mass object in a *de novo* sequence.

28. (previously presented) The method of claim 27, wherein each local mass-based alignment is generated with a breadth-first search, wherein all possible sequential combinations of mass objects of a specified number of mass objects are compared.

29. (previously presented) The method of claim 28, wherein said specified number of mass objects used in the breadth-first search is a search depth.

30. (original) The method of claim 29, wherein the search depth is 3-5.

31. (previously presented) The method of claim 21, wherein a breadth-first search is used identify the local mass-based alignment as either a mass match, a substitution, or a gap match.

32. (previously presented) The method of claim 31, wherein said breadth-first search first tries to identify a mass match, as a local mass-based alignment where the sum of the molecular masses of the consecutive mass objects in the sequence in the sequence database and the sum of the molecular masses of the consecutive mass objects in a *de novo* sequence are equal within a specified mass tolerance.

33. (original) The method of claim 31, wherein if there are no mass objects left on the side of the tag match in the sequence in the sequence database, a gap match is identified as a local mass-based alignment between a gap and at least one consecutive mass object in either the sequence in the sequence database or the *de novo* sequence.

34. (original) The method of claim 31, wherein if a mass match or a gap cannot be identified, then the breadth first search identifies a modification site as a local mass-based alignment where the sum of the molecular masses of the consecutive mass objects in the sequence in the sequence database and the sum of the molecular masses of the consecutive mass objects in a *de novo* sequence are not equal within a specified mass tolerance.

35. (original) The method of claim 31, wherein the number of mass objects in the *de novo* sequence and the number of mass objects in the sequence database is minimized.

36. (original) The method of claim 31, wherein the specified mass tolerance is designated by a mass tolerance of a tandem mass spectrometer device that generates the mass spectrometry data.

37. (previously presented) The method of claim 28, wherein after all fragments are matched in the breadth-first search in each respective sequence, a new local mass-based alignment is generated starting from next fragment following the last fragment that was matched in the *de novo* sequence and next fragment following the last fragment that was matched in the sequence in the sequence database.

38. (original) The method of claim 37, wherein a series of local mass-based alignments are made until the entire *de novo* sequence has been accounted for by the sequence in the sequence database in the mass-based alignments.

39. (previously presented) The method of claim 38, wherein a maximum number of consecutive modification sites are identified.

40. (previously presented) The method of claim 39, wherein the maximum number of consecutive modification sites is 1 or 2 local mass-based alignments in length.

41. (previously presented) The method of claim 39, wherein modification information is cataloged in a modification catalog.

42. (previously presented) The method of claim 41, wherein said modification information includes at least one of, molecular mass of the modification, specific fragments where the modification occurs, a frequency of occurrence of the modification at those fragments, wherein the frequency of occurrence is the estimated frequency in nature or a frequency as a sample preparation artifact, a mass object for the modification, which represents the additional mass of the modification to the *de novo* sequence at those fragments, the name of the modification, and a modification score for the modification.

43. (previously presented) The method of claim 42, wherein said modification is selected from, an *in vivo* or *in vitro* protein, a peptide modification, and an amino acid substitution.

44. (previously presented) The method of claim 43, further comprising: ranking the modification, wherein the ranking is based on its frequency of occurrence.

45. (previously presented) The method of claim 44, further comprising: identifying a most probable modification in the modification site from the modification catalog by matching elements to elements in modifications in the modification catalog

that are selected from at least one of, the mass difference, the fragments in the sequence database in the modification site, and the ranking of the modification in the modifications catalog.

46. (original) The method of claim 45, wherein the mass difference is the difference between the sum of the molecular masses of the consecutive mass objects in the sequence in the sequence database and the sum of the molecular masses of the consecutive mass objects in a *de novo* sequence in a local mass-based alignment.

47. (previously presented) The method of claim 45, wherein the mass object of an identified modification is inserted into the mass-based alignment, which creates a mass match between the *de novo* sequence and the sequence in the sequence database.

48. (previously presented) The method of claim 38, further comprising: computing a match score of each mass-based alignment, wherein the match score being a measure of how well the sequence in the sequence database matches the *de novo* sequence.

49. (previously presented) The method of claim 48, wherein said match score is generated from the linear combination of local alignment scores from the series of local mass-based alignments.

50. (original) The method of claim 49, wherein each of a series of consecutive local mass-based alignments receives a score and is classified.

51. (original) The method of claim 50, wherein each local alignment score is generated using a substitution matrix, depending on whether the local alignment is a mass match, a modification site, or a gap match.

52. (previously presented) The method of claim 51, wherein the substitution matrix contains a substitution matrix score of at least one fragment.

53. (previously presented) The method of claim 52, wherein the substitution matrix identity score is a substitution matrix score between a fragment and itself.

54. (previously presented) The method of claim 53, wherein the substitution matrix substitution score is a substitution matrix score between a fragment and a different fragment.

55. (previously presented) The method of claim 54, wherein the substitution matrix score is the log of the odds score of an identity of a fragment or a substitution between two fragments.

56. (previously presented) The method of claim 52, wherein the local alignment score for a mass match is the average value of the substitution matrix identity scores for all of the fragments in the sequence in the sequence database matched in the local alignment.

57. (previously presented) The method of claim 56, wherein if at least one of the fragments has been modified by a modification, the substitution matrix score for each modified fragment is the modification score for that modification.

58. (previously presented) The method of claim 52, wherein if the local mass-based alignment is a match between only one mass object from the sequence in the sequence database, and only one mass object from the *de novo* sequence, and ~~that~~ those mass objects represent single fragment, then the local alignment score for a substitution is the substitution matrix substitution score between the fragment in the sequence in the sequence database and the fragment in the *de novo* sequence.

59. (previously presented) The method of claim 52, wherein the local alignment score for a substitution is the number of fragments in the substitution in the sequence in the sequence database multiplied by the average value of the substitution matrix substitution scores.

60. (previously presented) The method of claim 52, wherein the local alignment score for a gap match is the number of fragments in the gap match in the *de novo* sequence multiplied by the average value of the substitution matrix substitution scores.

61. (previously presented) The method of claim 48, wherein if the termini of the *de novo* sequence are expected to be specific fragments, the match score is increased if the termini of the mass-based alignment match the expected specific fragments.

62. (previously presented) The method of claim 48, wherein if the termini of the *de novo* sequence are expected to be specific fragments, the match score is decreased if the termini of the mass-based alignment do not match the expected specific fragments, or if expected specific fragments are present inside the mass-based alignment.

63. (previously presented) The method of claim 1, further comprising utilizing an approach that interprets matches between sequences in the sequence database and said *de novo* sequence, which have been scored by a match score, as an identified macromolecule list and assigns a macromolecule score to each sequence in said identified macromolecule list.

64. (previously presented) The method of claim 63, wherein the match score is a measure of how well said sequences in the sequence database match the *de novo* sequence.

65. (previously presented) The method of claim 64, wherein a *de novo* sequence that matches at least one sequence in the sequence database is given a classification and inserted into a *de novo* sequence list, and the *de novo* sequence in the *de novo* sequence list is ranked by its delta score, which is the difference between the scores of the first and second best alignments for a given mass spectrum.

66. (original) The method of claim 65, wherein the delta score is computed for the de novo sequence as the difference between the match scores of the first and second matches to sequences in the sequence database for that de novo sequence. If that de novo sequence only matches one sequence in the sequence database, the delta score is the match score for that match.

67. (previously presented) The method of claim 66, wherein said classification is either a discriminating de novo sequence or a non-discriminating de novo sequence, wherein a discriminating de novo sequence is one that has a delta score greater than or equal to a delta score threshold and a non-discriminating de novo sequence is one that has a delta score less than a delta score threshold.

68. (original) The method of claim 67, wherein the delta score threshold for the *de novo* sequence is between 0% and 25% of the match score of the highest scoring match between a sequence in the sequence database and that *de novo* sequence.

69. (previously presented) The method of claim 67, wherein all matches between a sequence in the sequence database and a *de novo* sequence with match scores less than the match score of the highest scoring match between a sequence in the sequence database and that *de novo* sequence minus the delta score threshold are discarded.

70. (previously presented) The method of claim 69, wherein the sequence in the sequence database that matches best to the discriminating *de novo* sequence in said *de novo* sequence list with the greatest delta score is added to the identified macromolecule list, whereupon said *de novo* sequence is then moved from the *de novo* sequence list.

71. (original) The method of claim 70, wherein all non-discriminating *de novo* sequences in the *de novo* sequence list that match to that sequence in the identified macromolecule list are moved from the *de novo* sequence list to that sequence.

72. (previously presented) The method of claim 70, repeated until all discriminating *de novo* sequences in said *de novo* sequence list are removed from the *de novo* sequence list.

73. (original) The method of claim 72, wherein all sequences in the sequence database that match to non-discriminating *de novo* sequences still in the *de novo* sequence list are added to the identified macromolecule list, and the non-discriminating *de novo* sequences still in the *de novo* sequence list are moved to those sequences.

74. (original) The method of claim 73, wherein a macromolecule score is generated for every sequence in the identified macromolecule list.

75. (original) The method of claim 74, wherein the macromolecule score is a linear combination of the *de novo* macromolecule scores of the *de novo* sequences that have been assigned to that sequence.

76. (previously presented) The method of claim 64, wherein a new sequence database is generated and stored on a computer readable medium, containing only the sequences in the sequence database that are listed in the identified macromolecule list.

77. (previously presented) The method of claim 76, wherein *de novo* sequences that do not match any sequence in the original sequence database are re-analyzed by calculating a mass-based alignment between each *de novo* sequence in question and sequences in the new sequence database, in a way that the search space explored by the mass-based alignment algorithm is increased.

78. (original) The method of claim 77, further comprising: decreasing the specified length of tags.

79. (original) The method of claim 77, further comprising: increasing the search depth.

80. (original) The method of claim 77, further comprising: increasing the maximum number of consecutive substitutions.

81. (previously presented) The method of claim 64, wherein *de novo* sequences that do not match any sequence in the original sequence database are re-analyzed by calculating a mass-based alignment between each *de novo* sequence in question and sequences in a different sequence database.

82. (currently amended) A method for identifying sequences of a macromolecule having a sequence and sequence modifications thereof from mass spectrometry data comprising:

(a) providing at least one *de novo* sequence from mass spectrometry data of sequences of fragments of said macromolecule to a computer-based system that implements the identification of sequences of molecules and sequence modifications from mass spectrometry data,

(b) calculating at least one mass-based alignment between each *de novo* sequence and sequences in a sequence database, wherein the molecular masses of said fragments in a *de novo* sequence are compared to molecular masses of fragments in each sequence in the sequence database,

(c) interpreting mass differences between a sequence in the sequence database and the at least one *de novo* sequence using a modification catalog, said mass differences having been identified within said mass-based alignment,

wherein said modification catalog contains information for accurately identifying sequence variations and post-translational protein modifications,

(d) calculating at least one match score for the mass-based alignment that provides an indication of matching between the sequence in the sequence database and the at least one *de novo* sequence, and

(e) storing said score on a computer readable medium.

83. (original) The method of claim 82, further comprising: identifying sequences in the sequence database from mass-based alignments in response to the match scores.

84. (original) The method of claim 83, further comprising: grouping identifications of sequences in the sequence database from at least one *de novo* sequence into an identified macromolecule list that agrees with the *de novo* sequencing results.

85-90. (cancelled)